III B. Vehicular Traffic and Smoking

One major source of air pollution in general and of carbon monoxide in particular is automobile exhaust. Blood samples collected from vehicular drivers, traffic policemen, garage operators and miscellaneous workers show an increase in content of carboxyhemoglobin after exposure. The results of 19 investigations summarized in Table 5 indicate an overall average in 84 subjects of an increase of 1.1% of carboxyhemoglobin following 4 to 8 hours of exposure to vehicular traffic. The average peak level for 1,481 subjects was 3.9%.

The combination of exposure to vehicular traffic and cigarette smoking has been investigated by 8 groups and is summarized in Table 6. The peak blood levels showed an overall average of 6.8% of carboxyhemoglobin for 446 subjects. There is an increase of 2.9% in carboxyhemoglobin as a result of smoking and this value is close to the increase of 3.8% reported for subjects not exposed to vehicular traffic (see section IIB).

The most extreme example of combining cigarette smoking and exposure to automobile exhaust was reported by Srch (1967), who placed 4 subjects in an automobile with doors and windows closed inside a closed garage. Two of the subjects were smokers of 20 to 30 cigarettes daily, who were asked to smoke 5 cigarettes. Before smoking, the blood showed 5% of carboxyhemoglobin. After smoking 5 cigarettes, the blood levels had a mean value of 10%. The two nonsmokers in the automobile had 2% of carboxyhemoglobin before and 5% after the test. This situation rarely

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occurs in the ordinary course of events.

There is no reason to suspect that the blood levels of carboxyhemoglobin attained by the combination of cigarette smoking and exposure to vehicular traffice are responsible for the occurrence of vehicular accidents and poor driving (Boeck, 1958; Williams, 1964). The mechanical properties of the lung do not show any abnormality attributable to the exposure to cigarette smoking and vehicular traffic (Reichel et al, 1970). The incidence of sick rates among smokers was significantly higher than among nonsmokers who were exposed to carbon monoxide in the atmosphere (Fiandaca and Vercellotti, 1964; Mountain et al, 1968). There is a reduction in reaction time in drivers exposed to 90 minutes of commuting traffic (Ramsey, 1970). In all of these reports, although an elevation of carboxyhemoglobin is mentioned, a cause and effect relationship has not been established. The exposure to vehicular traffic is associated with inhalation of lead, ozone, hydrocarbons and nitrogen oxides, each of which can also contribute to the effect attributed to cabon monoxide alone. Literature on the toxicity of automobile exhaust is listed as additional bibliography No. 8.

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Table 5. Carboxyhemoglobin blood levels of nonsmokers following exposure to vehicular traffic.

Reference (Year)	Nature of subjects	No of Subjects	Carboxyhemoglobin Blood levels %		
			Before	After	
			Mean	Mean ± SD (Range)	Δ
Goldsmith, Terzaghi and Hackney (1963)	Los Angeles drivers	1	1.8	2.5	+10
Moureu (1964)	Paris vehicular drivers	597		4.5	
DeBruin, Bult and Van Haeringen (1965)	Amsterdam policemen	10	1.43	1.74	+0.3
DeBruin, Vroege and Van Haeringen (1965)	Rotherdam policemen	36	0.93	1.11	+0.08
Morando and Rovida (1965)	Genoa policemen	4		(1.83-4.00)	
Alivisatos, Bazas, Alexopoulos and Verykokakis (1967)	Athens residents	27	0		
Desoille (1967)	Paris garagemen	2		(2.3-3.5)	
Srch (1967)	Prague vehicular passengers	2		(2-5)	
Chovin (1967)	Paris policemen	7		1.25	
Ramsey (1967)	Dayton parking attendent	14	1.5	7.3 ± 3.46	+5.8
DeBruin (1967)	Amsterdam vehicular drivers	23	1.9	2.15	+0.25
Buchwald (1969)	Alberta garage operators	122		5.0	
Breysse and Bovee (1969)	Seattle fork lift drivers	92		1.2 (0-6)	
Gothe, Fristedt, Sundell, Kolmodin Ehrner-Samuel and Göthe (1969)	Stockholm policemen Malmo policemen Oreho policemen	28 6 3		1.2 ± 0.39(0.5-2.0) 0.8 ± 0.14(0.7-1.1) 0.6 ± 0.38 (0.4 -1.1)	
Szadkowski, Mastall, Schaller and Lehnert (1970)	Nuhrenberg dustmen	138		4.04 ±282	
Petrilli and Kanitz (1970)	Genoa vehicular drivers	20		(1.5-3.0)	
Cohen, Dorion, Goldsmith, Permutt(1971)	US-Mexican border inspectors	9	1.5	3.6	
Ayres and Buehler (1970)	New York pedestrians	1481		1.0	
Luderitz (1971)	Berlin policemen	120		(4-7)	
Mean (overall for number of subjects)				2.24 (2567 subjects)	+1.12 (84 subjects)

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Table 6. Carboxyhemoglobin blood levels of smokers following exposure to vehicular traffic.

Reference (Year)	Nature of subjects	No of subjects	Carboxyhemoglobin blood levels %				Net Δ compared
			Before	After smoking and exposure			
			Mean	Mean ± SD	(Range)	Δ	Nonsmoki
DeBruin, Bult and Van Haeringen (1965)	Amsterdam policemen	14	4.6	4.9		+0.3	+2.9
Chovin (1967)	Paris policemen	35	3.7				+2.5
Ramsey (1967)	Dayton parking atttendents	24	2.9	9.3 ± 3.16		+6.4	+2.0
Buchwald (1969)	Alberta garage operators						
	(1-9/day)	21		6.4	(1-15)		+1.4
	(10-20/day)	138		8.5	(0.5-19)		+3.5
	(>20/day)	76		9.2	(1-18)		+9.2
Breysse and Bovee (1969)	Seattle fork lift drivers						
	(<20/day)	44		3.5	(0-17)		+2.3
	(20-40/day)	38		5.5	(1-20)		+4.3
	(>40/day)	6		6.5	(3-14)		+5.3
Gothe, Fristedt, Sundell, Kolmodin, Ehrner-Samuel and Gothe(1969)	Stockholm policemen	28		3.5 ± 1.17			+2.3
	Malmo policemen	6		5.0 ± 2.4			+4.2
	Orebo policemen	5		2.4 ± 1.1			+1.8
Petrilli and Kanitz (1970)	Genoa vehicle drivers	20			(6.0-8.5)		
Cohen, Dorion, Goldsmith, Permutt (1971)	US-Mexican border inspector	11	4.8	6.4		+1.6	+2.8
Mean (overall for number of subjects)				6.8 (446 subjects)			+4.07 (446 subjec

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III. SOURCES OF CARBON MONOXIDE

B. Vehicular Traffic and Smoking

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IV. RESPIRATORY SYSTEM

It is not possible to determine the effect of the carbon monoxide portion of cigarette smoke on the respiratory system. The other constituents of cigarette smoke, i.e., nicotine and particulate material, are more likely to explain the reported effects of smoking on this system. The inhalation of mixtures containing carbon monoxide is a means of identifying its influence on respiration. The results are discussed below as acute effects in human subjects and in animals and as chronic effects in both. The techniques of analysis of carbon monoxide in the gaseous phase are summarized in additional bibliography No. 9. The application of carbon monoxide for measurement of lung function is covered in additional bibliography No. 10.

IV A. Acute Respiratory Effects in Humans

The inhalation of carbon monoxide does not stimulate respiration in man. Chiodi et al. (1941) tested a mixture of 0.15 to 0.35% carbon monoxide in air for 10 min. Although the carboxyhemoglobin level reached as high as 50%, there was no stimulation of breathing. Ayres et al. (1965) reported no consistent change in respiratory minute volume in 5 subjects with carboxyhemoglobin levels between 5 and 10%. Fisher et al. (1969) administered 6% carbon monoxide for 18 sec to each of 4 subjects. There were no changes in lung volumes, mechanical properties or diffusing capacity.

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Habitual smokers who also suffer from chronic lung disease are known to have an elevated carboxyhemoglobin level. Such patients show a reduction in pulmonary diffusion capacity (Chosy et al., 1963; Clauzel et al., 1966; Trinquet et al., 1971). Chevalier et al. (1966) compared such patients with nonsmokers inhaling 0.5% carbon monoxide. The resulting elevation in levels of carboxyhemoglobin caused a reduction in pulmonary diffusing capacity in nonsmokers. On this basis, it was proposed that the reduction in pulmonary diffusion capacity in smokers is due to elevation of the carboxyhemoglobin level. This explanation has not been supported by any other form of experimental data.

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IV B. Chronic Respiratory Effects in Humans

The medical examination of traffic officers stationed at the Holland Tunnell in New York has provided an opportunity to determine the effects of chronic exposure to 70 ppm carbon monoxide. Sievers et al. (1942) examined 156 such officers and failed to find any evidence of injury to health that was attributable to carbon monoxide exposure. There were no signs or symptoms of respiratory abnormalities. Other reports of elevated carbon monoxide levels in highway tunnels have appeared, but the clinical examination of the traffic officers has not been included (Braja and Trompeo, 1964; D'Arca et al. 1964; Miranda et al., 1967; Yamate and Matsumura, 1968).

Astrup et al. (1968) and Klausen et al. (1968) exposed 8 male subjects to inhalation of 0.5% carboxyhemoglobin, resulting in a blood level of 10%. There were no changes in ventilation, circulation or metabolism.

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IV C. Acute and Chronic Respiratory Effects in Animals

The lack of respiratory stimulation during acute exposure to carbon monoxide has also been demonstrated in animals (Korner, 1965). In perfusion of the carotid body chemoreceptors there was no evidence of direct stimulation by carbon monoxide (Duke et al., 1952; Joels and Neil, 1961; Meyer et al., 1972). With extremely high levels of carboxyhemoglobin a fall in blood oxygen tension occurs, which may cause activation of chemoreceptors. However, the respiratory centers are depressed directly by the reduction in blood oxygen content, so that chemoreceptor-induced hyperpnea is not apparent (Mills and Edwards, 1968).

Carbon monoxide in a concentration of 2% provokes bronchoconstriction in the guinea pig (Parrot et al., 1971). In the cat lung, ventilation with 1 to 20% carbon monoxide in air caused bronchodilatation with a fall in pulmonary arterial pressure (Duke and Killick, 1952). In the dog there is a rise in pulmonary arterial blood pressure following inhalation of carbon monoxide (Rubino, 1964). The differences in bronchomotor and pulmonary vascular responses between animal species have not been explained. Carbon monoxide is not toxic to bronchial cilia of various animals (Okeson and Divertie, 1970).

There are other differences in responses of various animal species. In the rat lung, exposure to 0.5 or 1.0% carbon monoxide in air caused swelling of alveolar epithelial mitochondria and nucleoplasm, swelling of capillary endothelial cells and capillary platelet thrombosis (Niden and Schulz, 1965). Mice exposed to carbon monoxide showed similar alteration

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in the alveolar tissue (Bils and Romanovsky, 1967; Rhodes, 1971). Experiments on the dog indicate that adminstration of a mixture of 8% to 14% carbon monoxide did not cause ultrastructural changes in the lung that could be attributed to the gas per se (Norman et al, 1966; Fisher et al, 1969). The observations on primates do not include electron microscopy. So far, the only published report based on gross and histopathological examination of lungs and other organs of the cynomolgus monkey does not reveal any abnormalities resulting from continuous exposure to 19.86 and 65.46 ppm carbon monoxide for 2 years (Eckardt et al, 1972).

The chronic exposure of animals to cigarette smoke reported by Dontenwill et al, (1966); Dontenwill (1967, 1970), and by Campbell (1936) does not relate directly to the effects of carbon monoxide alone. Experiments regarding exposure to automobile exhaust reported by Vaughan et al (1969) are difficult to interpret in terms of identifying the effects of carbon monoxide. Chronic exposure to carbon monoxide in air caused an aggravation of pulmonary tuberculosis in rabbits (Kiriachko, 1966) and did not influence the rate of tumor development in rats (Shintani, 1968).

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C. Acute and Chronic Respiratory Effects in Animals

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V. CIRCULATORY SYSTEM

The investigation of circulatory effects of carbon monoxide has been more extensive than that of its effects on the respiratory system discussed in the preceding section. There has been increasing concern that chronic exposure to carbon monoxide present in cigarette smoke would lead to diseases of the heart and blood vessels and abnormalities in the composition of the blood. However, the problem has not been solved by direct experimentation relating to the carbon monoxide in cigarette smoke. There are numerous observations regarding the effects of sublethal concentrations of carbon monoxide in man and animals. These are reviewed in the following paragraphs, although they are only remotely related to the small amount of carbon monoxide contained in cigarette smoke.

V A. Heart Rate

The acceleration of heart rate known to occur during inhalation of cigarette smoke is explained by the nicotine content. The amount of carbon monoxide in the smoke does not influence heart rate, since experiments consisting of administering carbon monoxide alone in amounts even exceeding that produced by cigarettes failed to alter the electrocardiogram.

The electrocardiograms of patients suffering from acute carbon monoxide poisoning or chronic exposure to carbon monoxide show the following alterations: depression of S-T segment (Steinmann, 1937; Störmer, 1938; Wendt, 1941; Graybiel, 1942; Breu, 1943; Patz, 1949; Saracoglu, 1951); sinus arrhythmia (Breu, 1942); premature systole (Parade and Franke, 1939); atrial flutter

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(Donatelli, 1940; atrial fibrillation (Dvorak et al., 1951; Cosby and Bergeron, 1963); distortion of QRS-T complex (Hegglin, 1944; Kostyukova, 1951; Lorente and Varela de Seijas, 1953) Wolff-Parkinson-White syndrome (Doumer and Merlen, 1946; Seling, 1966); atrioventricular block (Ehrich et al., 1944; Altmann, 1953; Kledecki and Winiarski, 1963); bundle-branch block (Graziani et. al., 1957); and cardiac arrest (Brunner, 1939). Multiple abnormalities in the electrogram have been reported (Faivre et al., 1954; Faivre et al., 1959; Capellaro and Gandolfo, 1964; Hayes and Hall, 1964; Medvedowsky et al., 1965; Shafer et al., 1965; Zanardi et al., 1966; Kuroiwa et al., 1968; Orinius, 1968; Lang et al., 1969; Mosinger et al., 1969; Lustman and Geerts, 1971; Thiels et al., 1972). Most of these abnormalities have been reproduced in animals inhaling concentrations larger than 2% carbon monoxide in air (von Bergmann, 1934; Motta, 1940; Loeper et al., 1942; Lewey and Drabkin, 1944; Hundt and Grunberg, 1960; Mainardi, 1964; Datsenko, 1966; Mosinger et al., 1969)

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